181 Definitions used for pulmonary exacerbation in clinical trials in cystic fibrosis (CF): a systematic review and meta-analysis

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Objectives: Literature reviews have identified a lack of consensus about the definition of an exacerbation in CF. We sought to determine which exacerbation definitions are most commonly used in CF clinical trials, and which signs/symptoms are most commonly included in exacerbation definitions across all CF clinical trials.
Method: Eligible randomised trials were those in people with CF aged over 6 years, where a sign/symptom-based definition was used to identify exacerbations as an outcome. Eligible trials were identified from reference lists of Cochrane Reviews in CF. Identified trials underwent citation tracking for further eligible trials. The number of times a definition was used across all trials was tallied. The number of times each symptom was included in any trial's definition was also tallied.
Results: The searches identified 36 trials that had clearly specified the exacerbation definition used. The most commonly used definitions were from the DNase trial by Fuchs (1994), used in 11 trials; the US CFF Conference (1994), used in 6 trials; and the EPIC study (2009), used in 3 trials. The symptoms most commonly used among all trials were: sputum (used in 36 trials), cough (35), spirometry (34), weight/appetite (33), chest sounds (29), CXR changes (29), fever (27) and dyspnoea (24). The remaining 13 signs/symptoms were each used in 18 or fewer trials.
Conclusion: Researchers may use these results to guide selection of a definition for their research. Clinicians may use these results to consider whether the definition used in a particular trial includes signs and symptoms that are generally accepted as representing an exacerbation by most clinical trialists in CF.

182 The impact of specific organisms and lung function on the frequency of respiratory exacerbations in paediatric CF patients

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Background: Respiratory exacerbations (RE) are an important outcome measure for research and clinical evaluation in Cystic Fibrosis (CF). Fuchs et al. proposed a standard definition of RE for CF, but there is little data regarding the rate of RE in CF. What evidence exists is inconsistent and fails to differentiate between hospitalized or non-hospitalized patients.
Objectives: To determine the RE rate (RER) in Pediatric CF patients and in specific CF pathologies.
Methods: A retrospective review of hospital admissions over a 1 year period (2010) were evaluated using Fuchs' RE criteria. These admissions were then examined for factors which might affect RER.
Results: Of 124 patients, 76 admissions were observed. 17 for non respiratory problems and 18 for 1st growth *Pseudomonas*. 41 admissions met RE criteria (RER per patient: 41/124 = 0.33). 5 (4%) patients had 14 admissions due to ABPA (RER = 2.8), 8 (6%) patients growing atypical mycobacteria, 2 admissions were observed (RER = 0.25), in 5 (4%) patients colonised with *Burkholderia cepacia* 2 admissions were recorded (RER = 0.4). 12 admissions were seen in 4 (3%) patients with severe disease (FEV1 <55%) (RER = 3.0), and 5 admissions in 7 (5%) patients who were non-compliant (RER = 0.7). In 45 patients aged 6–18 yrs considered stable 5 admissions were observed (RER = 0.11).
Conclusions: RE rates vary depending on underlying infection and clinical status. ABPA, atypical mycobacteria, *B. cepacia* and severe lung disease may increase risk of RE. When reporting RE, it is important to define criteria for RE, but also the CF population to which this measure is applied.

183 Impact of progression of cystic fibrosis lung disease on quality of life

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Background: Progression of Cystic fibrosis (CF) is characterized by bronchiectasis (BE) and small airways disease. CT is the gold standard to monitor progression of BE.
Hypothesis: Progression of BE results in a lower Health Related Quality of Life (HRQoL), assessed by the Cystic Fibrosis Questionnaire – Revised (CFQ-R).
Objective: To evaluate associations between changes in BE and in HRQoL over time.
Methods: Cohort study (July 2007–January 2012) in clinically stable children and adolescents with CF, with two routine bi-annual chest CTs combined with CFQ-Rs. CT scans were anonymized and randomly scored, using the CFCT-BE score, expressing BE as a % of a maximum score. CFQ-R was completed by children (aged 6–13 years) and their parents, or by adolescents (aged ⩾14 years). Score-range 0–100, higher scores indicate better HRQoL. For changes in CFCT-BE score and CFQ-R respiratory domain scores, correlations, and to test the hypothesis we respectively used Wilcoxon rank sum test, Student's paired t-test, Spearman's correlation coefficient, and a linear regression model, adjusted for age and gender.
Results: CF patients (n = 43): 31 children, 12 adolescents. In two years there was a significant change in CFCT-BE scores ($p = 0.03$), but not in CFQ-R scores ($p = 0.94$). At T_1 ($p < 0.01$, $r = -0.47$) and T_2 ($p = 0.01$, $r = -0.43$) CFCT-BE scores correlated to CFQ-R scores. Change in CFCT-BE scores did not correlate to change in CFQ-R scores ($p = 0.95$).
Conclusion: BE score correlates to HRQoL. A modest progression of BE does not result in impairment of HRQoL.
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184 Is chronic infection with methicillin resistant *Staphylococcus aureus* (MRSA) worse than methicillin sensitive *Staphylococcus aureus* (MSSA) in CF patients?

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The prevalence of MRSA infection is increasing in both the general population and CF patients. We hypothesized that MRSA infection is associated with more severe disease than MSSA infection in CF.
Objective: To compare clinical and functional features of CF patients chronically colonized with MRSA and MSSA.
Material and Methods: Observational, cross-sectional study. Clinical reports from patients attended at our Center during 2011 were reviewed. Age, gender, genetics, BMI Z-score, FEV_1, intravenous antibiotics were analyzed in chronically SA infection, positive to MRSA or MSSA (more than 50% of at least 4 sputum cultures during the year). Patients who were also colonized with *Pseudomonas aeruginosa* or *Burkholderia cepacia* were excluded.
Results: From 110 patients, 33 (30%) were chronically infected with SA (39% MRSA and 61% MSSA). From these, 10 patients in the MRSA group and 5 in the MSSA group were colonized with other bacteria, so they were excluded. In the MRSA group (7 females: 54%) the median current age was 8 years old (6 to 12 interquartile range) and in MSSA group (8 female: 40%) was 5 years old (3 to 10 interquartile range). In the MRSA group 46% had p.F508del mutation homozygous while 55% in MSSA group. The median BMI Zscore was –0.15 (–0.7 to 0.1) in the MRSA group and –0.06 (–0.4 to 0.3) in the MSSA group. (p = NS). The median FEV_1 was 75% (70 to 88) of predictive values in MRSA group and 99% (85 to 105) in MSSA group ($p = 0.03$). There were 1 (1 to 2) iv antibiotic courses in MRSA group and 0 (0 to 1) in MSSA group ($p = 0.01$).
Conclusion: CF patients chronically colonized with MRSA had a diminished pulmonary function and required more intravenous antibiotic courses.